UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,614	04/27/2006	Yvonne Paterson	P-7772-US	4019

49443 7590 07/05/2011

Pearl Cohen Zedek Latzer, LLP
1500 Broadway
12th Floor
New York, NY 10036

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
07/05/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO@pczlaw.com
Arch-USPTO@pczlaw.com

Office Action Summary	Application No.	Applicant(s)
	10/541,614	PATERSON ET AL.
	Examiner	Art Unit
	GINNY PORTNER	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,7-21,23 and 25-30* is/are pending in the application.

4a) Of the above claim(s) *9,10-19 and 27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7,8,20,21,23,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application
6)☐ Other: _____.

DETAILED ACTION

Claims 1-2, 5, 7-21, 23, 25-30 are pending.

Amended Claims 1-2, 5, 7-8, 20-21, 23, 25-26 are under consideration; all other claims stand withdrawn from consideration.

Election/Restrictions

1. Newly submitted claims 9 and 27 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: none of the examined methods previously recited the step of administering the bacterial vaccine vector to a human. All of the methods under examination were directed to enhancing the immunogenicity of a bacterial vaccine vector and not methods of administering a bacterial vaccine vector to a human for any reason to include stimulating an immune response.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 9, and 27 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Objections/Rejections Withdrawn

1. Withdrawn, Claims 1-2, 5, 7, 9, 20-21, 23, 25, 27 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, has been obviated by amendment of the claims to recite ----non-human animal---- thus obviating this rejection.
2. Withdrawn,Claims 1-2, 5, 7-9, 20-21, 23, 25-27 rejected under 35 U.S.C. 103(a) as being unpatentable over Pawelek (US Patent 6,685,935) in view of Vahidy et al (1996, reference cited on US PTO 1449) and Pan et al(1995, reference cited on US PTO 1449), is herein withdrawn in

light of applicant's amendment of the claims to recite the phrase "normal organ or normal tissue"; this phrase being the basis for new grounds of rejection being set forth below .

3. Withdrawn, Claims 1-2, 5, 7-9, 20-21, 23, 25-27 rejected under 35 U.S.C. 103(a) as being unpatentable over Pawelek (US Patent 6,685,935) in view of Vahidy et al (1996, reference cited on US PTO 1449) and Pan et al(1995, reference cited on US PTO 1449) is herein withdrawn in light of applicant's amendment of the claims to recite the phrase "normal organ or normal tissue"; this phrase being the basis for new grounds of rejection being set forth below .

Response to Arguments

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Maintained, The rejection of amended claims 1-2, 5, 7-9, 20-21, 23, 25-26 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is:

traversed by applicant by asserting the figures provide support for the instantly claimed genus of bacterial vaccine vectors that evidence the functional limitation "virulence of said vector is stabilized". Applicant points to the drawings as support for the functional limitations of the phrase "virulence of said vector is stabilized".

6. While the examiner agrees the drawings show the bacterial load can be maintained over 1 or 2 passages before infectivity can start to decline, the drawings do not provide original descriptive support nor teach which and/or how many virulence factors are being stably expressed in the bacteria of the figures. While the figures may show the bacterial vaccine

vector's ability to infect cells can be maintained, the figures do not provide support for the stable expression of any and all virulence factors expressed by Listeria monocytogenes, which is what is now claimed. The claims require continuous stabilized expression of the vaccine vector's virulence factors, but based on the nature of Listeria to escape from a cell vacuole into the cytosol of the infected cell, one of skill in the art would expect the levels of virulence factors and the types of virulence factors to change, thus all Listeria virulence factors would not be stably expressed. Author Lemes-Marques et al (FEM S microbiology letters, 2004, see page 64 column 1, paragraph 1) teach that environmental conditions on Listeria monocytogenes cause great variation in the expression of virulence factors, therefore variation in expression of virulence factors is a part of Listeria's infection life cycle; thus all of Listeria's virulence factors are naturally not continuously/stably expressed .

2. Upon further consideration of the instant Specification the examiner found at page 15, lines 1-6 of instant Specification, the specification to teach the

a. "Bacterial clones that retain the ability to express such antigens and/or fusion proteins are then selected for the next round of bacterial replication. The skilled artisan, when equipped with the methods disclosed herein will therefore be able to select a bacterial vaccine vector that stably and predictably expresses a heterologous antigen and/or fusion protein."

7. The instant specification teaches the selection of a vaccine vector that stably and predictably expresses a **heterologous antigen or fusion protein**, the heterologous antigen and /or fusion protein is/are not taught to be a Listeria/bacteria vaccine vector's virulence factor but a

heterologous expression product. Therefore the instant specification once again does not provide original descriptive support for the phrase "virulence of said vector is stabilized".

8. All of the claims have been newly amended to recite a sub -genus of species of bacterial vaccine vectors that have the functional characteristic set forth by the phrase "virulence of said vector is stabilized" which does not evidence original descriptive support in the instant Specification. All of the claims still recite New Matter for the reasons set forth above.

1. Applicant's arguments with respect to claims 1-2, 5, 7-9, 20-21, 23, 25-26 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person *having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the* manner in which the invention was made.

3. Claims 1-2, 5, 7-8, 20-21, 23, 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vahidy et al (1996, reference cited on US PTO 1449) in view of Pan et al(1995, reference cited on US PTO 1449).

4. Vahidy et al teach a process for animal passaged Listeria monocytogenes which results in increased viability counts per gram of infected organ with each passage wherein (see Figure 2, page 141, top of column 1) increased viability was found to be a function of infectivity (colonies per gram of infected organ) and virulence operon activation (see page 142, col. 1, paragraph 2, middle of paragraph), the method of Vahidy et al comprising the steps of :

5. Instant claims 1, 2, 7, 20, 21,25:

a. administering to a non-human animal (rabbit, a mammal) a Listeria monocytogenes (see page 139, col. 2, last paragraph "Infection was produced by intravenously inoculating 1ml of a saline suspension of fresh cultures of L. monocytogenes"),

b. passaging the Listeria through the animal (see page 140, col. 1, p. 3)

c. harvesting the Listeria monocytogenes from a normal organ or normal tissue (liver, spleen or brain (see page 140, col. 1, paragraph 2 and 2 "recovered"),

d. repeating steps a), b) and c) with the harvested Listeria until a maximum bacterial virulence in said organ or tissue is reached (see Figure 2, passages V1-V6) page 141, col. 2, p. 3 "Virulence of all cultures was also tested in the present study in rabbit models. Lethality and bacterial load of organs were employed as criteria for pathogenicity") and virulence is stabilized (see page 141, col. 2, p. 3 "onset of death was more prompt (less than 24 h) and infection was more severe as the magnitude of colonization of the liver, spleen and brain intensified"; see page 140, col. 1, p. 3 last sentence "Further passage was not carried out as hemolysin and lecithinase production was greatly reduced by the sixth passage").

Vahidy et al teach the claimed methods steps but differs from the instantly claimed invention by failing to show the Listeria monocytogenes to express a heterologous tumor antigen and the non-human mammal to be a mouse.

6. Pan et al teach a recombinant Listeria that express a heterologous tumor antigen and shows the recombinant Listeria monocytogenes to induce a protective cytolytic T-cell (see Figure 4, title) response when engineered to stably express a foreign/heterologous antigen which stimulates an immune response to the expressed antigen (see abstract and entire article) in mice

in an analogous art for the purpose of showing Listeria monocytogenes can effectively express a heterologous antigen upon administration to a non-human animal. Pan et al. showed that recombinant Listeria monocytogenes has the ability to deliver a foreign/**heterologous** antigen to the immune system and to involve cell-mediated immunity against the same antigen." Pan et al., 1995, "A recombinant Listeria Monocytogenes vaccine expressing a model tumour antigen protects mice against lethal tumour cell challenge and causes regression of established tumours", Nature Medicine 1:471-477. "

It would have been obvious to the person of ordinary skill in the art at the time the invention was made modify the method of Vahidy et al with the Listeria monocytogenes bacterial vaccine vector of Pan et al, because Vahidy et al teach that through animal passage of Listeria monocytogenes the count per gram of infected organ increases to maximum load levels which would provide for stimulation of an enhanced immune response to an encoded heterologous antigen taught by either Pan et al (tumour antigen).

It also would have been obvious to the person of ordinary skill in the art at the time the invention was made to transform Listeria monocytogenes with the heterologous gene coding sequence of an antigen as taught by Pan et al to carry out animal passaging to maximum load as taught by Vahidy et al because Vahidy et al teaches through maximum load animal passaging increased infectivity results and enhanced survival providing for an extended period of time for expression of the encoded heterologous antigen.

It is prima facie obvious to make a simple substitution of one known equivalent element, the known Listeria monocytogenes strain of Pan et al for the Listeria monocytogenes strain of Vahidy et al, for another in a method of passaging for reaching maximum virulence infective/

maximum load as taught by Vahidy et al, to obtain predictable results of increased expression of the heterologous tumor antigen of Pan et al due to increased number of Listeria monocytogenes per normal organ or tissue achieved through carrying out the repeated methods steps of as taught by Vahidy et al. Vahidy et al in view of Pan et al obviate the instantly claimed invention as now claimed.

Conclusion

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/
Examiner, Art Unit 1645
June 10, 2011

/Mark Navarro/
Primary Examiner, Art Unit 1645